



### **Amendments to the Specification**

Please replace the paragraph at page 7, line 27 through page 8, line 3 with the following amended paragraph:

---**Fig. 1.** Sequence Alignment of Nit Proteins with a Plant Nitrilase.

The Nit domains of *C. elegans* (SEQ ID NO:15) and *D. melanogaster* (SEQ ID NO:14) NitFhit proteins are aligned with Nit homologs from *H. sapiens* (SEQ ID NO:1 and SEQ ID NO:12), *M. musculus* (SEQ ID NO:2 and SEQ ID NO:13), *S. pombe* (SEQ ID NO:6 and SEQ ID NO:7), *S. cerevisiae* (SEQ ID NO:4 and SEQ ID NO:5), *X. laevis* (SEQ ID NO:3), and Nitrilase1 from *A. thaliana* (SEQ ID NO:11). Secondary structural elements and sequence numbers correspond to worm NitFhit. The figure was prepared with ALSCRIPT (Levitt, M., Chothia, C., *Nature* 261:552-558, 1976). Human Nit2 (SEQ ID NO:1), murine Nit2 (SEQ ID NO:2), frog Nit1 (SEQ ID NO:3), and budding yeast Nit2 and Nit 3 (SEQ ID NO: 4 and SEQ ID NO:5, respectively) are newly cloned and have been deposited in Genbank with accession numbers VVV, WWW, XXX, YYY and ZZZ. Carets mark the positions of insertions that are found in some of the sequences. Residues found in the vicinity of Cys 169 are indicated by filled circles.---

Please replace the paragraph at page 13, line 20 through page 14, line 11 with the following amended paragraph:

---In the course of cloning Fhit homologous cDNAs from *D. melanogaster* and *C. elegans*, NitFhit sequences were identified (Pekarsky, Y. et al., *Proc. Natl. Acad. Sci.* 95:8744-8749, 1998). The Nit domain of the invertebrate NitFhit proteins was classified as a distinct member of the nitrilase superfamily and used to clone the single most homologous sequences from human and mouse cDNA libraries (Pekarsky, Y. et al., *Proc. Natl. Acad. Sci.* 95:8744-8749, 1998). It has been pointed out that events that fuse unrelated proteins (Marcotte, E.M., et al., *Science* 285:751-753, 1999; Enright A., et al., *Nature* 402:86-90, 1999) are most likely to be functionally significant (Marcotte, E., et al., *Nature* 402:83-86 1999) if the separate proteins have

similar gene expression patterns and have similar phylogenetic profiles (Pellegrini, M., et al., *Proc. Natl. Acad. Sci. USA* 96:4285-4288, 1999). At the level of tissue-specificity, murine *Fhit* and *Nit1* have nearly identical mRNA accumulation profiles (Pekarsky, Y. et al., *Proc. Natl. Acad. Sci.* 95:8744-8749, 1998). Therefore, identification of Nit-related genes from divergent organisms known to contain Fhit-homologous genes, namely *S. cerevisiae* and *S. pombe* (Brenner, C., et al., *Natl. Struct. Biol.* 4:321-238, 1997) and *X. laevis*, was sought. In each yeast, two Nit-related sequences were identified (**Fig.1; SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6 and SEQ ID NO:7**), as well as sequences related to plant nitrilases. The frog also yielded a Nit sequence and further examination of human and murine expressed sequence tag databases allowed for the identification of a second Nit coding sequence from human and mouse (**Fig. 1; SEQ ID NO:1 and SEQ ID NO:2, respectively**). Nit sequences have a low level of identity with nitrilases and a substantial level of identity with each other. Nit homologs, having been found fused or coordinately expressed with Fhit homologs (Pekarsky, Y., et al., *Cancer Research* 58:3401-3408, 1998) and in the same organisms as Fhit homologs (**Fig. 1; SEQ ID NOS:1-15**), are reasonable candidates for proteins that interact with Fhit homologs.---

**Figures**

Enclosed, please find three original color replacements and one annotated copy for Fig. 1 to address the Examiner's comment that the sequences identified in Fig. 1 of the application do not represent the sequences disclosed as SEQ ID NOS. in the Sequence Listing (Office Action, page 2, paragraph 2). The amino acid sequences designated Hs\_Nit2, Mm\_Nit2, Sp\_Nit2, Sc\_Nit3, Xl\_Nit1, Sp\_Nit1, Sc\_Nit2 and At\_Nitrilase 1 in Fig.1 have been amended to add additional amino acids to the end of each respective sequence, such that the sequences in amended Fig. 1 correctly represent the sequences disclosed in the Sequence Listing, as filed.